Renal Isotransplantation without Immunosuppression

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Four renal isografts have been performed and all have had satisfactory function for 7½ to 17⅔ years without prophylactic or therapeutic immunosuppression. Three of these patients originally had glomerulonephritis, and in one there was histologic evidence of recurrent disease, 7½ years after transplantation, without proteinura and without change in renal function. Although this experience is small, it suggests that prophylactic immunosuppression is not appropriate for recipients of renal isografts.

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BETWEEN 1954 AND 1965 THE BOSTON experience with 22 renal transplants from presumed identical twins included 17 recipients with probable subacute or chronic glomerulonephritis.[4,8–10,13] Eleven of these 17 patients developed in their isotransplanted kidneys glomerular disease which was thought to represent recurrent glomerulonephritis. It was suggested by the authors that prophylactic or therapeutic immunosuppression is beneficial in preventing or treating recurrent glomerulonephritis.[4]

In Denver, no immunosuppression has been given to the four recipients of identical twin kidney transplants who are the subject of this report.

Clinical Material and Results

Between January, 1962 and Feburary, 1972, four patients received kidney transplants in Denver from presumed identical twin donors. None have received prophylactic or therapeutic immunosuppressive agents of any kind and none have received prophylactic antibiotics since transplantation.

Three of the four patients had chronic glomerulonephritis originally and one had chronic pyelonephritis (Table 1). These diagnoses were confirmed histologically in the three patients whose own kidneys (and spleens) were removed at the time of transplantation. The first recipient still has his original kidneys and he has declined to have his transplanted kidney biopsied.

All four patients have good kidney function, with recent (1978/1979) serum creatinines less than 1.5 mg/dl and creatinine clearances of at least 60 ml/min and no proteinuria (Table 1). The renal function in all patients has been stable essentially since the time of transplantation.

Renal Biopsy Results

In 1978 three patients had open biopsies of their transplanted kidneys. One of the biopsied patients (HO) originally had chronic pyelonephritis. Her biopsy, done 12 years after transplantation, revealed a normal kidney. Biopsies in two patients who originally had chronic glomerulonephritis revealed a normal transplant in one (FR) and recurrent glomerulonephritis in the other (JB).

The patient with recurrent disease received her transplant in 1972, six years before the biopsy was done; the changes in the biopsy specimen (Fig. 1) resembled the type 1 mesangiocapillary glomerulonephritis found in her own kidneys at the time of nephrectomy in 1972. Light microscopy showed some generalized increase in the number of mesangial cells, slight segmental thickening of the glomerular capillary walls and an increase in the amount of mesangial matrix. Immunoperoxidase revealed generalized and diffuse granular deposits of IgG, IgM, IgA, C3, C1q and C4 in the mesangium and in the capillary walls. Ultrastructurally, the capillary basement membranes were segmentally thickened by large subendothelial collections of finely granular electron dense material and by circumferential mesangial cell interposition. The mesangium also contained deposits of electron dense material. Immuno-

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TABLE 1. *Clinical Characteristics of Four Patients with Renal Isografts*

Patient	Date of Transplant	Original Disease	Bilateral Nephrectomy, Splenectomy	Current Creatinine Clearance	Current Proteinuria	1978 Renal Biopsy
JW	Jan. 1962	CGN	No	85 ml/min	0	None*
FR	July 1963	CGN	Yes	110 ml/min	0	Normal
HO	April 1966	Pyelo.	Yes	60 ml/min	0	Normal
JB	Feb. 1972	CGN	Yes	60 ml/min	0	Recurrent glomerulonephritis

* Patient declined.

electronmicroscopy confirmed that the immunoglobulins and complement were located in the subendothelial and mesangial deposits. Analysis of this patient's serum obtained in August 1978 revealed a low total hemolytic complement (48%; normal range 60–140) but normal C3, C1q and C4, and no nephritic factor (C3 NeF). The C1q binding assay[16] showed that immune complexes consisting of IgG, IgM and C3 were present. DNA binding was normal. There is no clinical evidence of infection in this patient. Urine culture for cytomegalovirus in August 1978 was negative. This patient has had no detectable proteinuria.

Discussion

The first successful renal isograft was performed in Boston in 1954; 28 additional cases had been done at the Peter Bent-Brigham Hospital by March, 1976.[10] Seventeen of the original 22 renal isograft patients had glomerulonephritis, and recurrent disease was diagnosed in 11 of these 17 patients; seven of the 11 patients with recurrent disease died 0.5 to 99 months after transplantation, and the recurrence was considered a major contributing cause in six of the seven deaths.[4] Three of the 17 patients with glomerulonephritis received pro-

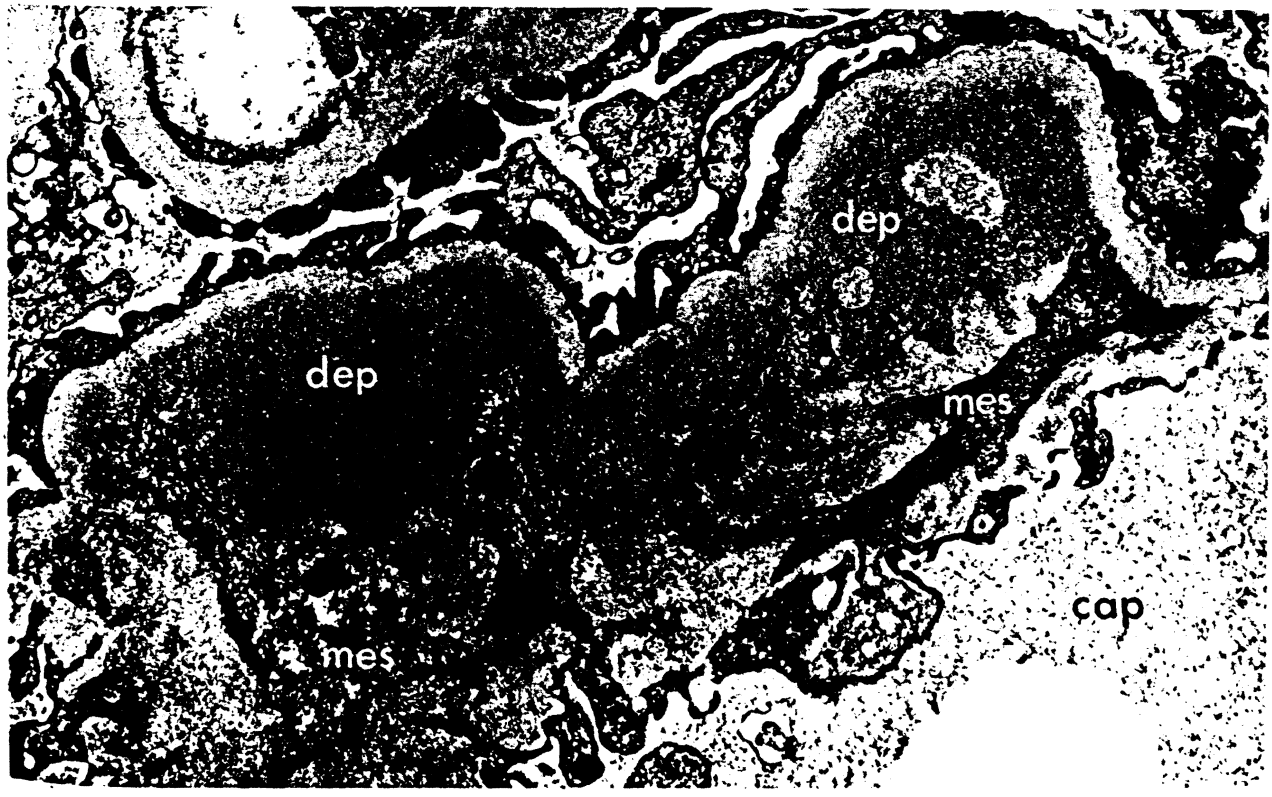

FIG. 1. Electron micrograph of part of a glomerular capillary loop from patient JB's renal isograft. There are two large subendothelial deposits (dep) on the capillary basement membrane and there is mesangial cell interposition (mes) in the capillary wall. cap = capillary lumen (×13,940).

phylactic immunosuppression beginning at or near the time of transplantation: one developed recurrent disease two days after transplantation and died two weeks after transplantation, and two have had no recurrence. Six patients received immunosuppressive treatment following discovery of recurrent glomerulonephritis: four died after 4–27 months of immunosuppressive therapy without improvement in renal function, and two patients survived without significant improvement in renal function.[4,8]

In Japan there were three cases of recurrent glomerulonephritis in the first 5 isografts done there, and Tagaki recommended the use of small doses of prophylactic azathioprine to try to prevent recurrence;[5] however there is no clear evidence to suggest that this approach would in fact lower the recurrence rate.

The histologic differentiation of recurrent disease from rejection can be extremely difficult in renal allografts[3,6,12] but in renal isografts it is assumed that rejection is not operative and that any histopathologic changes are due to mechanisms other than rejection. In our patient with recurrent mesangiocapillary glomerulonephritis without proteinuria, the clinical significance of the immunopathologic findings is uncertain. Histologic recurrence of type 1 mesangiocapillary glomerulonephritis is known to be consistent during a long period with good transplant function, particularly when there is no clinical or urinary abnormality.[11]

The possibility that host nephrectomy may reduce the frequency of recurrent glomerulonephritis is difficult to assess in our patients. One of our three patients with chronic glomerulonephritis has not had his own kidneys removed and has no clinical evidence of recurrent disease 17⅔ years after transplantation (no biopsy done); on the other hand, our one patient with recurrent disease did have her own kidneys removed at the time of transplantation. In the Boston experience the time of removal of the patient's own kidneys did not influence recurrence.[8]

The possible benefit of prophylactic antibiotics, to prevent streptococcal infection and nephritis, is also difficult to assess in our patients. None of our four patients were treated with prophylactic antistreptococcal agents. Some of the Boston patients received prophylactic antibiotics,[9] but the role of streptococcal infection in the genesis of recurrence in their patients was not established.[4]

The likelihood that the four Denver patients would have had better clinical courses with than without prophylactic immunosuppression seems small. All three of the patients who originally had chronic glomerulonephritis have had good graft function for 7½ to 17⅔ years since transplantation, with current creatinine clearances of 60–85 ml per minute. Furthermore, it is not unlikely that so many years of immunosuppression would have been associated with complications of immunosuppression such as Cushing's syndrome, aseptic necrosis, or cataracts.[14]

The poor response of the six Boston patients to immunosuppression started after the onset of recurrent glomerulonephritis,[4] and the uncertain value of immunosuppression of glomerulonephritis in nontransplanted kidneys[1,2,7,15] have disuaded us from subjecting our patient who has recurrent disease without proteinuria to the risk of immunosuppression.

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